available at www.sciencedirect.com

SCIENCE DIRECT®

www.elsevier.com/locate/brainres

BRAIN RESEARCH

Research Report

Tryptophan-deficient diet increases the neurochemical and behavioral response to amphetamine

Manolo Carta, Fabio Fadda, Roberto Stancampiano*

Department of Sciences Applied for Biosystems, Section of Physiology and Human Nutrition, University of Cagliari, Via Porcell 4, I-09124 Cagliari, Italy

ARTICLE INFO

Article history:
Accepted 23 March 2006
Available online 24 May 2006

Keywords:
Tryptophan
Striatum
Nucleus accumbens
Serotonin
Dopamine release
Locomotor activity

Abbreviations:
5-HT, serotonin
DA, dopamine
VTA, ventral tegmental area
NAcc, nucleus accumben
TRP, L-tryptophan
5-HIAA, hydroxyindolacetic acid

ABSTRACT

The present study examined the effects of a tryptophan-deficient diet on behavioral and neurochemical response to amphetamine. A tryptophan-deficient diet (14 days) decreased striatal serotonin and 5-hydroxyindolacetic acid content in rats. Under the latter conditions, amphetamine increased dopamine efflux in striatum and nucleus accumbens and produced a greater increase in motor activity when compared to controls. These results indicate how response to psychostimulants might be altered in the presence of a tryptophan-deficient diet.

1. Introduction

An increasing number of studies provide evidence for a modulatory influence of serotonin (5-HT) on dopaminergic system, suggesting that 5-HT receptors may represent an important target in improving the therapeutic approach to neuropsychiatric disorders related to mesolimbic or nigrostriatal dopaminergic dysfunctions (Deutch et al., 1991; Meltzer and Nash, 1991; Henderson et al., 1992; Roth and Meltzer, 1995; Kapur and Remington, 1996; Barnes and Sharp, 1999).

Enhanced dopamine (DA) neurotransmission, particularly in the mesolimbic dopaminergic system, plays an important role in mediating the locomotor and reinforcing effect of psychomotor stimulants (Sharp et al., 1987; Di Chiara and Imperato, 1988; Ichikawa and Meltzer, 1992; Wise, 1995). Serotonergic projections arising from dorsal raphe to the substantia nigra and ventral tegmental area (VTA), as well as to the striatum (Olpe and Koella, 1977; Jacobs and Azmitia, 1992) and nucleus accumbens (NAcc) (Azmitia and Segal, 1978; Herve et al., 1987; Van Bockstaele et al., 1996) modulate

* *Corresponding author*. Fax: +39 070 6758917.
E-mail address: ffadda@unica.it (F. Fadda).

0006-8993/$ – see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.brainres.2006.03.118

dopaminergic transmission (Herve et al., 1979; Nedergaard et al., 1988; Kapur and Remington, 1996).

It is noteworthy that changes in 5-HT tone are capable of altering the effect elicited by psychostimulants. Generally speaking, pharmacological manipulations that decrease central serotonergic transmission potentiate psychostimulant-induced locomotor activity in rats, while activation of the serotonergic system appears to inhibit this effect (Cannon et al., 1976; Asin and Fibiger, 1983; Morrow and Roth, 1996; Herges and Taylor, 1999). Accordingly, serotonergic tone appears to be strongly implicated in the effect of psychostimulants.

The brain content of 5-HT can be modified by means of dietary manipulation of L-tryptophan (TRP) (Fernstrom, 1983; Young et al., 1989), the precursor of 5-HT. Indeed, administration of a TRP-deficient diet produces a specific and long lasting reduction of 5-HT content throughout the whole rat brain (Biggio et al., 1974; Gessa et al., 1975) and in the concentration of extracellular 5-HT in hippocampus and cortex (Stancampiano et al., 1997; Fadda et al., 2000). For these reasons, a TRP-deficient diet is extensively used when depleted brain 5-HT levels are required and offers a specific non-toxic tool with which to study the role of 5-HT in the brain (Fadda, 2000). However, to date, the effect of a TRP-deficient diet on the behavioral and neurochemical effects produced by psychostimulants remains to be studied.

In the present study, we used a TRP-deficient diet, a unique non-pharmacological tool for use in the study of 5-HT/DA interaction, formulated to provide a very low TRP content, in order to investigate the net effect of decreased brain serotonin levels on amphetamine-induced motor activity and DA release in striatum and NAcc.

2. Results

2.1. *Striatal content of DA, 5-HT and 5-hydroxyindolacetic acid*

As shown in Table 1, 14 days consumption of the TRP-deficient diet induced a significant decrease in striatal content of 5-HT (61%) and 5-hydroxyindolacetic acid (5-HIAA) (68%). The TRP-deficient diet did not significantly affect DA content in this brain area.

2.2. *Extracellular concentration of DA in the striatum and NAcc*

Basal extracellular levels of DA, collected from striatum and NAcc, uncorrected for probe recovery, did not differ between the two experimental groups and were 152 ± 11 (control) and 160 ± 14 (TRP deficient diet) fmol/20 min sample, and 42 ± 5.3 (control) and 47 ± 5.7 (TRP deficient diet) fmol/20 min, respectively. Fig. 1 shows the effect of amphetamine (2 mg/kg i.p.) on DA release in control and TRP deficient rats. ANOVA analysis for DA release revealed a significant difference between the

Table 1 – Effect of a TRP-deficient diet on DA, 5-HT and 5-HIAA concentration in the striatum (pmol/mg of wet tissue)

	DA	5-HT	5-HIAA
Control	55.23 ± 7.15	2.22 ± 0.31	1.87 ± 0.21
TRP-deficient rats	53.98 ± 5.14	0.85 ± 0.22*	0.59 ± 0.31*

Values are mean ± SEM of six animals.
* $P < 0.05$ vs. control rats.

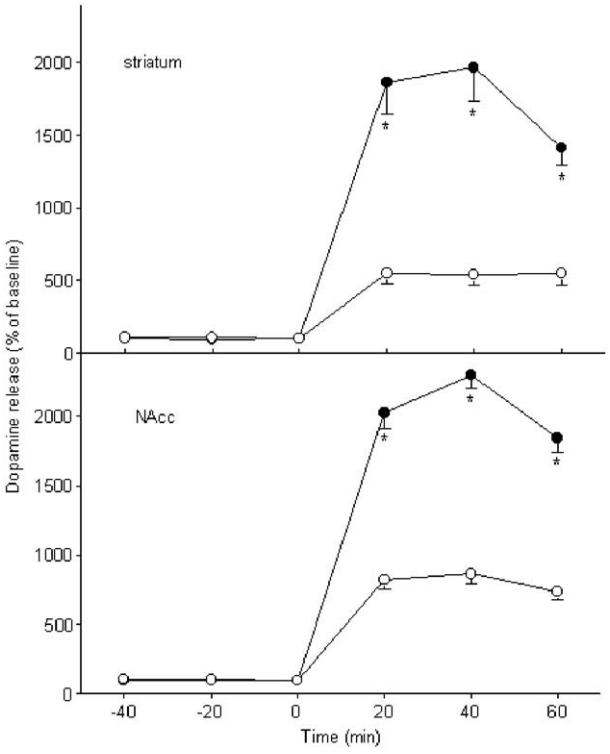

Fig. 1 – Effect of amphetamine administration (2 mg/kg i.p., time = 0) on the extracellular level of dopamine in TRP deficient (●) and control (○) rats. Data points represent the mean ± SEM ($n = 6$) percentage changes from basal release. *$P < 0.05$ vs. control in corresponding time.

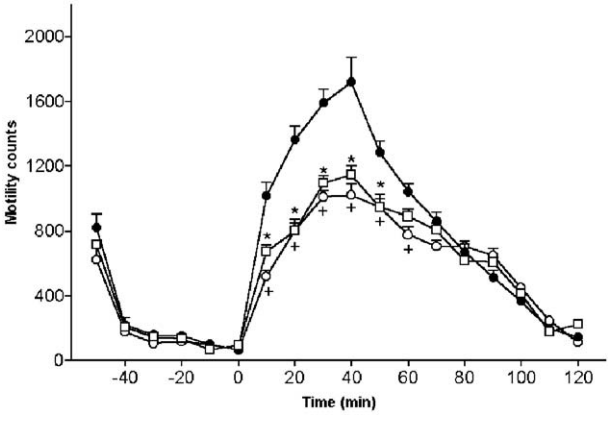

Fig. 2 – Motility induced by amphetamine (2 mg/kg i.p., time = 0) in TRP-deficient (●), TRP replenished (□) and control (○) rats. Each point represents the mean value ± SE of 12 rats. Data are expressed as activity counts (total number of photocells beam interruption) per 10 min. +,*$P < 0.05$ vs. control in corresponding time.